UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,266	04/25/2006	Huy Ong	20747/240	4952

7590 12/04/2007

Edwin V Merkel
Nixon Peabody
Clinton Square
P O Box 31051
Rochester, NY 14603

EXAMINER	
MACFARLANE, STACEY NEE	
ART UNIT	**PAPER NUMBER**
1649	

MAIL DATE	DELIVERY MODE
12/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,266	ONG ET AL.	
	Examiner	Art Unit	
	Stacey MacFarlane	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6 and 26-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6 and 26-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Sequence compliance

1. This application contains sequence disclosures that are encompassed by the definitions for amino acid sequences set forth in 37 C.F.R. § 1.821 (a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825. Specifically, no sequence identification has been provided for the amino acid sequences presented in claim 6 of the instant specification. In case this sequence is new, Applicant needs to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO: X) be made in the specification and claims wherever a reference is made to that sequence. See M.P.E.P. 2422.04.

Election/Restrictions

2. Applicant's election without traverse of Group I, claims 1-3, 6 and 26-28, in the reply filed on October 19, 2007 is acknowledged.

Claims 4, 5 and 16-25 have been cancelled.

Claims 1-3, 6 and 26-28 will be considered upon their merits in the instant office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 2 and 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claim 2 recites the limitations "such plaques, hypercholesterolemia or cardiovascular disease". There is insufficient antecedent basis for the limitations "hypercholesterolemia" or "cardiovascular disease" in the claim.

5. Claim 3 is vague and indefinite in its recitation of a method comprising "treating pre-existing atherosclerosis ... to a patient who has atherosclerosis".

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 26 recites a growth hormone releasing peptide of Hexarelin family, a derived peptidomimetic or a CD36 ligand. Claim 27 recites a GHRP derivative, a derived peptidomimetic or a CD36 ligand. Claim 28 recites a GHRP derivative or a derived peptidomimetic. The claims do not require that the Hexarelin family peptide, derived peptidomimetic or CD36 ligand possess any particular conserved structure or other disclosed distinguishing feature. Thus the claims are drawn to a genus of molecules that is merely defined by function and the instant specification fails to describe the entire genus of molecules that are encompassed by these claims.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant is in possession of specific examples of GHRP releasing hormone peptides (paragraph 0006), derivatives (paragraph 0062), peptidomimetics (paragraph 0039) and CD36 ligands (paragraph 0042). The claims, however, encompass method of administration of any peptide within the Hexarelin family, any derivative or peptidomimetic or any CD36 ligand, thus, the claims are not limited to specific molecules with known structure. The claims merely require the claimed methods employ molecules that modulate the expression of CD36 and/or ABCA1.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factor present in the claim is a recitation of activity. There is not even identification of any particular portion of the structure that must be conserved for activity. As stated above, it is not even clear what molecules except hexarelin and EP80317 are members of the GHRP releasing hormone peptide family, derivatives or peptidomimetics thereof, and/or CD36 ligands. The specification does not provide a complete structure of derivatives, peptidomimetics or ligands and fails to provide a representative number of species for the recited genus. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, the court clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the

encompassed within the genus of GHRP releasing hormone peptide family, derivatives or peptidomimetics thereof, and/or CD36 ligands, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of identifying activity. Adequate written description requires more than a mere recitation of activity as part of the invention and a reference to a potential method of isolating or screening. The compound itself is required. See *Fiers v Revel*, 25 USPQ2d 1601 at 1601 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification only provided for the bovine sequence.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-3, 6 and 26-28 are rejected under 35 U.S.C. 102(a) as being anticipated by Broglio et al. *European Journal of Pharmacology*, 448:193-200, May 10, 2002.

9. Claim 1 is drawn to a method of treatment or prophylaxis of atherosclerosis comprising administration of one or more Growth Hormone Releasing Peptides (GHRPs) to a patient in need. Dependent claims further limit the patient: a patient at risk of developing such plaques, hypercholesterolemia or cardiovascular disease (Claim 2), or a patient "who has atherosclerosis" (Claim 3); and further limit the GHRPs as hexarelin or EP80317 (a.k.a. Tyr-Ala-hexarelin) (Claim 6). Claims 26-28 are drawn to a peptide of Hexarelin family or GHRP derivative. Absent active steps by which modulation of expression is achieved, Claims 27-28 do not further limit the instant method but merely recite inherent results of administering a GHRP derivative.

10. The Broglio prior art teaches methods of treatment and/or prophylaxis of atherosclerosis comprising hexarelin administration to a patient in need thereof. The patient population within the Broglio reference are patients with coronary artery disease receiving by-pass surgery. The diagnosis of coronary artery disease was based on a history of prior myocardial infarction and evidence of coronary artery lesions as determined by angiography (page 194, section 2.1). Patients were administered hexarelin, which the instant disclosure has defined as fulfilling the requirements encompassed by the terms “Growth Hormone Releasing Peptide”,

"peptide of Hexarelin family", "GHRP derivative" and "CD36 ligand" of the instant claims. Thus, the method of Broglio anticipates the instantly claimed method.

11. The Broglio reference does not recite the effects of modulation of expression of CD36 and/or ABCA1, however, since the claims merely recite administration of hexarelin as the sole active step of the method, then absent methodological steps that further define the process by which modulation of expression is to be performed, these are taken to encompass inherent results from the sole step of drug administration.

MPEP § 2112 provides guidance as to the Examiner's burden of proof for a rejection of claims under 35 U.S.C. 102 or 103 based upon the express, implicit, and inherent disclosures of a prior art reference. The case law clearly states that something which is old does not become patentable upon the discovery of a new property.

> "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999).

Thus, the claiming of a new use, new function or unknown property that is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). Further, *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the

same DNA sequence as the claimed oligonucleotides. The court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." *Id.* In addition the court has held that there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention."); *Abbott Labs v. Geneva Pharms., Inc.*, 182 F.3d 1315, 1319, 51 USPQ2d 1307, 1310 (Fed.Cir.1999).

The case law specifically applies to the instant application where Applicant has claimed a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference. In the instant case, Applicant's invention is directed to methods comprising the active step of administering hexarelin to patients that are in need of treatment and/or prophylaxis of atherosclerosis, defined as at risk of developing lesions or who has atherosclerosis. The examiner has applied prior art which disclosed methods comprising administering hexarelin to an identical patient population. The examiner's assertion of inherency is based upon the structural similarity

between the patented composition and the claimed composition and the identical requirements of patient population.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established and the burden of proof rests upon the Applicant to demonstrate that the prior art does not necessarily or inherently possess the characteristics of Applicant's claimed product. *In re Fitzgerald*, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

12. Claims 1, 2, 6 and 26-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Imbimbo et al. *European Journal of Clinical Pharmacology*, 46: 421-425, May 1994, as evidenced by the American Heart Association (AHA), Heart and Stroke Statistics—2002 Update.
13. The Imbimbo prior art teaches administration of hexarelin to male subjects. In light of the AHA 2002 report that states 90% of the population as at least one risk factor for cardiovascular disease (i.e. high blood cholesterol, tobacco use, physical inactivity, overweight, or diabetes mellitus) then one of ordinary skill in the art could reasonably assert that the methods of the prior art teach the instantly claimed

method of administration for prophylaxis. Thus, the prior art anticipates the method of the claims.

Conclusion

14. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacey MacFarlane whose telephone number is (571) 270-3057. The examiner can normally be reached on M, W and Alt. F, 6 am to 3 pm, T & R 5:30 am - 4 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner

Art Unit 1649

/SNM/

OLGA N. CHERNYSHEV, PH.D.
PRIMARY EXAMINER